Remarks and Arguments

Status of the Claims

Claims 15-16, 18, 21-26 and 29 are pending and stand rejected.

Amendments to the Claims

Claim 16 has been amended to recite that the bacterial infection or bacterial-related disease is selected from periodontal disease or sinusitis. This feature was previously recited in claim 17, now canceled.

Claim 18 has been amended to preserve proper dependency.

Claim 29 has also been amended to recite that the bacterial infection or bacterial-related disease is selected from periodontal disease or sinusitis. Support for this amendment is found in previously pending claim 17, now canceled.

Claim 22 has been amended to delete recitation of the phrase "or fragment or derivative thereof."

Claims 27, 30 and 31 are hereby canceled.

No new matter is introduced as a result of these amendments. Applicant respectfully requests that the present amendments be entered under 37 C.F.R. §1.116 since the present amendments either cancel claims, adopt Examiner suggestions, remove issues for appeal, and/or require only a cursory review by the Examiner.

Each of the present amendments to the claims is made without prejudice, and Applicant reserves the right to pursue any subject matter canceled as a result of these amendments in future prosecution, either in this application or in one or more continuing applications.

Claim Rejections Under 35 U.S.C. §112, First Paragraph

Written Description

Claims 27, 30 and 31 were rejected under 35 U.S.C. §112, first paragraph for lack of written description. Without conceding the merits of the rejection, claims 27, 30 and 31 have

been canceled, rendering this rejection moot. Applicant thus respectfully requests withdrawal of this rejection.

Enablement

Claims 16-18, 21-27, and 29-31 were rejected under 35 U.S.C. §112, first paragraph for lack of enablement. Specifically, the Examiner asserts that the specification, while being enabling for a method of treating a mammal suffering from gingivitis comprising administering a therapeutically effective amount of a GM-CSF polypeptide, does not enable treating any bacterial-related disease by administering a composition comprising a GM-CSF polypeptide, or a fragment or derivative thereof.

As discussed above, claims 27, 30 and 31 have been canceled, rendering this rejection moot as it applies to these claims. Additionally, claim 22 has been amended to delete recitation of the phrase "or fragment or derivative thereof," rendering this rejection moot inasmuch as it pertains to such fragments or derivatives.

Without conceding the merits of the rejection, claims 16 and 29 have been amended to recite that "the bacterial infection or bacterial-related disease is selected from periodontal disease or sinusitis," rendering the outstanding enablement rejection moot.

Applicant takes this opportunity, however, to correct the record. The Examiner asserts that the specification only discloses treating periodontal disease by locally administering GM-CSF. This is not correct. The specification in fact successfully exemplifies **two diverse, unrelated bacterial diseases**, periodontal disease and chronic sinusitis (see Examples 1 and 2), that can be treated using the presently claimed methods and compositions. Chronic sinusitis is a localized bacterial infection that can be treated in accordance with the presently claimed methods and compositions, but it is not a periodontal disease. Applicant thus submits that the present specification enables treatment of a **broad genus** of localized bacterial diseases by administration of a GM-CSF polypeptide.

Moreover, as discussed in the response filed November 7, 2008, upon reading the specification, one of ordinary skill in the art would certainly know which sites in the body are amenable to local administration of a GM-CSF polypeptide for treating a localized bacterial

infection, a bacterial related disease, or both, and would be able to employ suitable techniques and reagents to effect such localized administration without any undue experimentation.

Nevertheless, solely to expedite prosecution of the present application, independent claims 16 and 29 have been amended to recite that "the bacterial infection or bacterial-related disease is selected from periodontal disease or sinusitis." Applicant asserts that the presently pending claims comply with the enablement requirement of 35 U.S.C. §112, first paragraph and respectfully requests withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. §112, Second Paragraph

Claim 30 was rejected under §112, second paragraph as being indefinite. Without conceding the merits of this rejection, claim 30 is hereby canceled, rendering this rejection moot. Applicant thus respectfully requests withdrawal of this rejection.

Claim Rejections Under 35 U.S.C. §103

Grabstein et al. in view of Grzybowski et al.

Claims 16, 21-27 and 29-31 were rejected under 35 U.S.C. §103 as being obvious over Grabstein *et al.* (U.S. Patent No. 5,162,111) in view of *Grzybowski et al.* (Int. J. Pharmaceuticals 184, pp. 179-187, 1999). As discussed above claims 27, 30 and 31 have been canceled rendering this rejection moot as it applies to these claims. Moreover, independent claims 16 and 29 have been amended to recite that "the bacterial infection or bacterial-related disease is selected from periodontal disease or sinusitis." This feature was recited in previously pending claim 17, now canceled. Without conceding the merits of this rejection as applied to previously pending claims 16, 21-27 and 29-31, Applicant submits that the rejection under 35 U.S.C. §103 over Grabstein *et al.* in view of *Grzybowski et al.* is rendered moot with respect to the currently pending claims, and respectfully requests its withdrawal.

Grabstein et al. in view of Grzybowski et al., further in view of Sampathkumar

Previously pending claims 17 and 18 were rejected under 35 U.S.C. §103 as being obvious over Grabstein *et al.* (U.S. Patent No. 5,162,111) in view of *Grzybowski et al.* (*Int. J.*

Pharmaceuticals 184, pp. 179-187, 1999), further in view of Sampathkumar (U.S. Patent No. 4,804,530).

The Grabstein *et al.* reference is cited for teaching that bacterial infection can be treated with systemic application of GM-CSF. The Grzybowski *et al.* reference is cited for teaching that dressings containing GM-CSF can be prepared that are suitable for applying to a wound to stimulate healing.

The Examiner acknowledges that neither Grabstein *et al.* nor Grzybowski *et al.* teach or suggest treating a localized bacterial infection or bacterial related disease selected from a periodontal disease or sinusitis. The Examiner cites Sampathkumar for teaching that diseases such as periodontal disease involve bacterial infection, and asserts that this teaching cures the deficiencies of Grabstein *et al.* and *Grzybowski et al.* Applicant traverses this rejection.

As an initial matter, Applicant submits that Grzybowski *et al.* do not teach treating localized bacterial infection with GM-CSF. Instead, Grzybowski *et al.* only teach that dressings containing GM-CSF can be prepared and that GM-CSF affects *in vitro* phagocytic activity of peripheral blood human leukocytes (see page 183, first column). Importantly, Grzybowski *et al.* only treat bacterial infections *in vivo* using **G-CSF, not GM-CSF.** As is known to those of ordinary skill in the art, G-CSF and GM-CSF are distinct proteins with distinct activities and effects. See e.g., http://www.multiplemyeloma.org/treatments/3.07.03.php, a copy of which is attached to this Response. Grzybowski *et al.* even highlight the differences between the two proteins, stating that "The antimicrobial effect of rhG-CSF does not necessarily mean that this cytokine will accelerate healing of the all types wounds [sic] *in vivo*. In fact, Jyung and co-workers were not able to detect any significant effect of the recombinant rat G-CSF (rrG-CSF) on the healing process of the wounds in rats whereas rrGM-CSF led to the markedly enhances healing..." (see page 185, second column). As such, Grzybowski *et al.* teach that G-CSF, which they used to treat bacterial infection, is **not equivalent** to GM-CSF as recited in the presently pending claims. Thus, the disclosure of Grzybowski *et al.* in fact points towards non-obviousness of the presently claimed methods and compositions.

The disclosure of Sampathkumar is directed to pharmaceutical compositions comprising anaerobe-selective antibacterial agents which are substituted or unsubstituted 1,12-dodecanedioic peroxy acids, or their pharmaceutically-acceptable salts or esters (see e.g., Abstract). Nowhere,

however, does Sampathkumar teach or suggest methods comprising **local administration** of therapeutically effective amounts of **GM-CSF** to treat **periodontal disease or sinusitis**, or compositions for such local treatment of periodontal disease or sinusitis comprising therapeutically effective amounts of GM-CSF, as recited by the currently pending claims.

There is no motivation to combine the antibacterial chemical agents of Sampathkumar with the teachings of either Grabstein *et al.* or Grzybowski *et al.* Moreover, even if one were to combine the teachings of Grabstein *et al.*, Grzybowski *et al.* and Sampathkumar, such combination would not result in the methods and compositions of the presently pending claims: references teaching systemic administration of GM-CSF, use of dressings containing G-CSF, and pharmaceutical compositions comprising 1,12-dodecanedioic peroxy acids cannot be combined to result in local administration of GM-CSF to treat periodontal disease or sinusitis.

Applicant thus respectfully requests withdrawal of this rejection.

In light of the present amendments and arguments, Applicant submits that the present application is in condition for allowance, and respectfully requests a notice to that effect. If the Examiner feels that it would further prosecution or expedite allowance of the present case, she is invited to telephone the undersigned at 612-766-2071

Applicant believes no fees are required with this filing. However, please charge any fees, or apply any credits or previous overpayments, to deposit account 06-1050, referencing Attorney Docket No. 15665-0010US1.

Respectfully submitted,

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